



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/PT99/00015 <b>(22) International Filing Date:</b> 17 August 1999 (17.08.99)  <b>(30) Priority Data:</b> 102197 21 August 1998 (21.08.98) PT  <b>(71) Applicant (for all designated States except US):</b> INSTITUTO NACIONAL DE ENGENHARIA E TECNOLOGIA INDUSTRIAL/INSTITUTO DE BIOTECNOLOGIA, QUÍMICA FINA E TECNOLOGIAS ALIMENTARES [PT/PT]; Azinhaga dos Lameiros, Paço do Lumiar, P-1699 Lisboa Codex (PT).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> MEIRINHOS DA CRUZ, Maria, Eugénia [PT/PT]; Rua Maestro Raúl Ferrão, 43, P-1500 Lisboa (PT). CARVALHEIRO, Manuela, Colla [PT/PT]; Avenida Almirante Reis, 62-G, 4º, P-1150 Lisboa (PT). JORGE, João, Carlos, Santana [PT/PT]; Rua Acácio Pereira, 8, R/C A, Olivais Sul, P-1800 Lisboa (PT).  <b>(74) Agent:</b> ARNAUT, José, Luís; Rua do Patrocínio, 94, P-1399-019 Lisboa (PT).	<b>(81) Designated States:</b> BR, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
<b>(54) Title:</b> DINITROANILINE LIPOSOMAL FORMULATIONS AND PROCESSES FOR THEIR PREPARATION		
<b>(57) Abstract</b> <p>The invention refers to liposomal formulations containing one or several dinitroanilines, varying the liposome size from 50 µm to 0.01 µm with encapsulation efficiencies typically bigger than 30 %. When administered to animals, the liposomal dinitroanilines do not present acute toxicity or significantly diminish the toxicity of the free formula and are effective against infections by protozoarian or other microorganisms. The present invention refers also to a process for the preparation of liposomal formulations that comprises the preparation of multilamellar liposomes containing the dinitroaniline, to submit them to dehydration, rehydration and, optionally, to a sizing step before the dehydration. The dehydration is carried out in the presence of cryoprotectants in order to avoid sublimation and consequent loss of the drug in this step. The present invention refers also to dinitroaniline liposomal formulations containing a mixture of particles that after sizing, present populations superior and inferior to 100 nm in diameter.</p>		